

IN THE SPECIFICATION:

Please replace paragraph 1 of the specification with the following amended paragraph:

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This application is a continuation-in-part of U.S. Patent Application No. 08/485,458, which issued as U.S. Patent No. 5,705,385 on January 6, 1998, and of U.S. Patent Application No. 08/484,282, which issued as U.S. Patent No. 5,981,501 on November 9, 1999.

REMARKS

Claims 42 and 44-75 are pending in the above-referenced patent application. The specification has been amended to update the status of all applications to which priority is claimed. No new matter has been added by the amendments to the specification.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

The Invention

Novel lipid-nucleic acid particles which are useful for *in vitro* or *in vivo* gene transfer are provided by the present invention. The particles can be formed using either detergent dialysis methods or methods that utilize organic solvents. Upon removal of a solubilizing component (*i.e.*, the detergent or the organic solvent), the lipid-nucleic acid complexes form particles, wherein the nucleic acid is serum-stable and is protected from nuclease degradation.

Rejection under 35 U.S.C. § 102(e)

Claims 42 and 44-75 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 5, 820,873 ("Choi *et al.*"). In view of the following remarks, Applicants respectfully traverse the rejection.

To anticipate a claim, a reference must disclose each and every element of the challenged claim and must enable one skilled in the art to make the anticipated subject matter.

See, *PPG Industries Inc. v. Guardian Industries Corp.*, 37 USPQ2d.

Claim 42 of the present invention is directed to a nucleic acid-lipid particle comprising a cationic lipid, a conjugated lipid that inhibits aggregation of particles, and a nucleic acid, ***wherein the nucleic acid in the nucleic acid-lipid particle is resistant in aqueous solution to degradation with a nuclease.***

As stated on page 4, lines 29-31, of the specification, the nucleic acid-lipid particles of the present invention are constructed in a way such that upon removal of a solubilizing component (*i.e.*, the detergent or the organic solvent depending on which methods is employed), the ***nucleic acid becomes protected from nuclease degradation.*** The nucleic acid-lipid particles thus formed are suitable, *inter alia*, for use in intravenous nucleic acid transfer as they are stable in circulation, of a size required for pharmacodynamic behavior resulting in access to extravascular sites, and target cell populations.

Choi *et al.* teach a novel class of polyethylene glycol modified ceramide lipids, *i.e.*, PEG-ceramide conjugates, that can be used to form liposomes and other lipid formulations containing various biological agents or drugs.

The Office Action alleges that the liposomes disclosed by Choi *et al.* produce particles that meet the structural limitations of the particles produced by the methods of the instant invention and are, therefore, presumed to have the same functional properties as the particles produced by the method of the present invention. Applicants respectfully disagree and, in doing so, direct the Examiner's attention to the Declaration of Michael J. Hope, Ph.D. ("the Hope Declaration"), a copy of which is attached. It is noted that the original Declaration of Michael J. Hope Ph.D. was filed in corresponding U.S. Patent Application No. 09/566,700.

As set forth by Dr. Hope in his Declaration, if the methods disclosed by Choi *et al.* were used to load (or encapsulate) nucleic acid into the liposomes disclosed

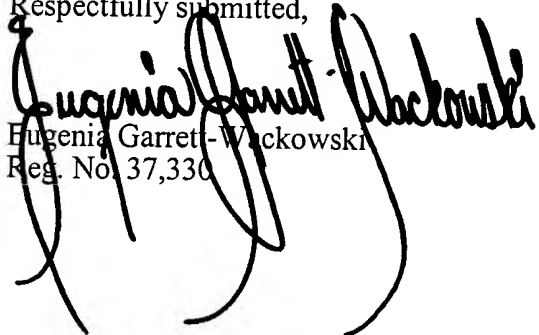
therein, such methods would *not* result in nucleic acid-lipid particles that fully encapsulate the nucleic acid in the lipid portion (*e.g.*, in the liposome) such that the nucleic acid is resistant in aqueous solution to degradation with a nuclease. Instead, it is Dr. Hope's opinion that using the loading methods disclosed by Choi *et al.*, the nucleic acid would *not* be fully encapsulated in the liposome and, thus, it would be susceptible in aqueous solution to degradation with a nuclease.

In view of the foregoing remarks and Dr. Hope's Declaration, Choi *et al.*, which discloses methods for preparing and loading classical (or traditional) liposomes, do *not* teach the nucleic acid-lipid particles of the present invention, wherein the nucleic acid in the nucleic acid-lipid particles is resistant in aqueous solution to degradation with a nuclease. As Choi *et al.* do *not* disclose each and every aspect of the claimed invention, it cannot form the basis of a proper anticipation rejection. Accordingly, the anticipation rejection under 35 U.S.C. § 102(e) over Choi *et al.* is improper and should be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 925-472-5000.

Respectfully submitted,


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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Paragraph 1 of the specification has been amended as follows:

This application is a continuation-in-part of U.S. Patent A[a]pplication [serial] N[n]o. 08/485,458, which issued as U.S. Patent No. 5,705,385 on January 6, 1998, and of U.S. Patent A[a]pplication [serial] N[n]o. 08/484,282, which issued as U.S. Patent No. 5,981,501 on November 9, 1999 [both filed on June 7, 1995].